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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/502,403	06/20/2005	Jose Manuel Francisco Ochoa	2099.0090000/VLC/UWJ	3497

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EXAMINER	
RAE, CHARLESWORTH E	

ART UNIT	PAPER NUMBER
1611	

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01/06/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/502,403	OCHOA, JOSE MANUEL FRANCISCO	
	Examiner	Art Unit	
	CHARLESWORTH RAE	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 October 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,6,8 and 11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,6,8 and 11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's arguments, filed 10/24/08, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set of actions being applied to the instant application.

This action is final. The finality of the action is necessitated by the amendment narrowing the scope of the claimed amount of glimepiride and metformin.

Status of the Claims

Claims 1, 4, 6, 8, and 11 are currently pending in this application.

Claim Amendment

Applicant's claim amendment, received 10/24/08, is acknowledged and made of record.

Response to applicant's arguments/remarks

Rejection under 103(a)

This rejection is withdrawn in view of the claim amendment and applicant's persuasive arguments.

Rejection under 102(b)

Applicant's arguments with respect to claims 1, 3-9 and 11have been considered but are moot in view of the new ground(s) of rejection. It is noted that the Timmins et al.

is being maintained as the primary reference and that the merits of this reference will be discussed below.

REJECTIONS

Claim rejections – 35 USC 103(a)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 4, 6, 8, and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Timmins et al. (US Patent 6,031,004), in view of Langtry et al. Glimepiride: a review of its use in the management of type 2 diabetes mellitus. Drugs. 1998;55(4):563-584, abstract only).

Timmins et al. (US Patent 6,031,004) teach a method for treating diabetes comprising administering formulations comprising a metformin salt (e.g. hydrochloride salt, fumarate salt, or succinate salt) by itself or in combination with another oral

antidiabetic agent such as a sulfonylurea urea e.g. glimepiride, wherein the compositions have improved taste properties to enhance patient compliance (col. 2, lines 26-36; col. 3, lines 6-50; and reference claim 15). Timmins et al. exemplify formulations comprising antihyperglycemic combinations of metformin and a sulfonylurea and methods of treatment using said combinations for treating hyperglycemia in patients with Type II diabetes, wherein glimepiride is disclosed as a preferred sulfonylurea antihyperglycemic agent for use in combination with metformin, and wherein the metformin/sulfonylurea are used in a ratio of 300/1 to about 50:1 (col. 1, lines 7-12; col. 3, lines 28-50; col. 4, lines 33-35; cols. 5-10, especially Examples 5, 6, 7, 8;). Timmins et al. also disclose that metformin has a bitter taste and is usually marketed as a coated tablet (col. 1, lines 29-35). Timmins et al. teach that **the most preferred metformin product is the hydrochloride salt (also known as Glucophage**; col. 2, lines 17-21). Also, Timmins et al. teach compositions comprising a pharmaceutically acceptable carrier (e.g. see reference claim 5). In addition, Timmins et al. teach that the dose administered must be carefully adjusted according to the age, weight, condition of the patient, route of administration, dosage form and regimen, to achieve a desired result (col. 4, lines 59-67).

Although Timmins et al. teach tablet formulations comprising metformin and glimepiride in a weight ratio of 300:1, this reference does not teach the specifically instantly claimed ratio of metformin:glimepiride (500:1) or the specific dose amounts of glimepiride and metformin hydrochloride recited in claims 6, and 11.

Langtry et al. teach that the dosage of glimepiride is usually started at 1 mg/day, titrated to glycaemic control at 1-2 week intervals to a usual dosage range of 1 to 4 mg/day (abstract).

It would have been obvious to a person of skill in the art at the time the invention was made to manipulate the dose amount of metformin hydrochloride and glimepiride as taught by Timmins et al., including applicant's dosage amount, based on patient parameters such as age, weight, and severity of hyperglycemia in order to control the blood glucose in said patient with diabetes.

Further, it would have been obvious to a person of skill in the art at the time invention was made to combine the teachings of the cited references to modify the dose of glimepiride in metformin/glimepiride combination as taught by Timmins based on teaching of Langtry et al. of glimepiride in a dose amount of 1-6 mg to treat a patient with type 2 diabetes. One would have been motivated to do so because Timmins et al. teach formulations comprising metformin and a sulfonylurea (e.g. glimepiride) for treating type 2 diabetes and Langtry et al. suggest that glimepiride may be used in combination with other antidiabetic agents to control glucose in doses of 1-6 mg. (see In re Kerkhoven, 205 USPQ 1069 (CCPPA 1980). Further, glimepiride 1.2 mg as taught by Langtry et al. in combination with 600 mg of metformin salt (e.g. metformin hydrochloride) as taught by Timmins et al. would result in a formulation comprising glimepiride/metformin salt in a weight ratio of 1/500, which is identical to the instantly claimed weight ratio. The motivation for combining the components flows from their individually known common utility. Besides, it is the examiner's position that it is routine

in the medical and pharmaceutical arts to manipulate the weight ratios of active ingredients in combination formulations used to treat type 2 diabetes based on in patient parameters factors as patient's age, weight, and severity of diabetes to order to optimize blood glucose control. Hence, one would reasonably expect that the prior art compositions comprising metformin salt/glimepiride in overlapping ratio amounts would exhibit similar synergistic properties as the instant claimed compositions since the treatment population encompassed by the instant claims is identical to the population of the prior art (claims 1 and 8).

It is noted that the instant specification discloses pharmaceutical compositions comprising 500 mg of metformin clorhidrate and 2 mg of Glymepirid (specification, page 9, Example 2), which overlaps with the teaching of Timmins et al. of compositions comprising metformin/glimepiride in amounts ranging from 50:1 to 300:1.

It is noted that Timmins et al. teach tablet and capsule formulations which read on the term "[a] solid pharmaceutical composition" as recited in, for example, claim 1 and the term "in a solid dosage form" as recited in claim 8.

With respect to the term "at least one excipient" as recited in claims 4, 6, Timmins et al. teach compositions comprising a pharmaceutically acceptable carrier which is considered to be an excipient (e.g. see reference claim 5).

With respect to the preamble of claim 8, it is noted that Timmins et al. also teach a method for treating diabetes.

Thus, it would have been obvious to a person of skill in the art at the time the invention was made to create the instant claimed invention with reasonable predictability.

Response to applicant's arguments/remarks

Applicant's argument that Timmins et al. do not teach metformin hydrochloride is not found to be persuasive because even though Timmins states that the other salts are preferred, Timmins does not teach that the prior art hydrochloride salt does not work as evidenced by the commercial use of the hydrochloride salt (Glucophage). See col. 2, lines 17-21. Furthermore, "a known or obvious composition does not become patentable simply because it has been described as somewhat inferior to some other product for the same use." In re Gurley, 27 F.3d. 551, 554, 31 USPQ 2d. 1130, 1132 (Fed. Cir. 1994). Although applicant correctly points out that Timmins et al. do not teach metformin hydrochloride/glimepiride ratio of 500:1, it is the examiner's position that it would have been obvious to a person of skill in the art to manipulate the dosage of amount of metformin/glimepiride as taught by the prior art, including the instant claimed dose ratio, based on patient parameters such as age, weight, and severity of hyperglycemia, to control blood glucose levels within the normal range since blood glucose levels varies significantly from patient to patient. Besides, Timmins et al. teach metformin/glimepiride ratio of 50:1 to 300:1 which overlaps with applicant's disclosed pharmaceutical compositions comprising 500 mg of metformin clorhidrate and 2 mg of Glymepirid (specification, page 9, Example 2). See applicant's Response, pages 10-11.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charlesworth Rae whose telephone number is 571-272-6029. The examiner can normally be reached between 9 a.m. to 5:30 p.m. Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila G. Landau, can be reached at 571-272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http:pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 800-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

27 December 2008
/C. R./
Examiner, Art Unit 1611

/Sharmila Gollamudi Landau/

Supervisory Patent Examiner, Art Unit 1611